

SUPPORT FOR THE AMENDMENTS

Support for the amendment to Table 1 beginning on page 5, line 7, is found at specification page 4, lines 22-30, page 5, lines 1-6, and original Table 1 beginning on page 5, line 7.

The present amendment cancels claims 1-11, and adds new claims 12-31.

Support for newly added claim 12 is found at specification page 1, lines 4, 23-24 and 28, as well as original claim 1.

Support for newly added claim 13 is found at specification page 2, lines 15-18, as well as original claim 2.

Support for newly added claims 14 and 15 is found at specification page 3, lines 14-16, as well as original claims 4 and 5.

Support for newly added claim 16 is found at specification page 2, lines 24-25, as well as original claim 3.

Support for newly added claims 17 and 18 is found at specification page 2, lines 12-14 and 19-26.

Support for newly added claims 19-31 is found at specification page 1, lines 25-30, page 2, lines 1-11, and page 4, lines 5-14, as well as original claims 6-11.

It is believed that these amendments have not resulted in the introduction of new matter.

REMARKS

Claims 12-31 are currently pending in the present application. Claims 1-11 have been cancelled, and new claims 12-31 have been added, by the present amendment.

Applicants wish to extend their appreciation to Examiner Davis for the helpful and courteous discussion held on July 31, 2009, with their undersigned Representative. During the meeting, the prior art rejection was discussed, with a particular emphasis on evidence of superior properties, as set forth in the present specification, and arguments based on rulings established in U.S. case law, for overcoming the rejections. The content of this discussion is believed to be reflected in the remarks set forth herein.

The rejection under 35 U.S.C. § 103(a) of now cancelled claims 1-11 as being obvious over Buck (U.S. Patent 2,400,038) in view of Carenzi (U.S. Patent 4,764,530) is respectfully traversed with respect to new claims 12-31.

Applicants have discovered that the claimed ibopamine maleate salt having a molar ratio of ibopamine to maleate of 1:1 remarkably exhibits improved tolerability, as compared to the conventional ibopamine hydrochloride salt described and exemplified in Carenzi.

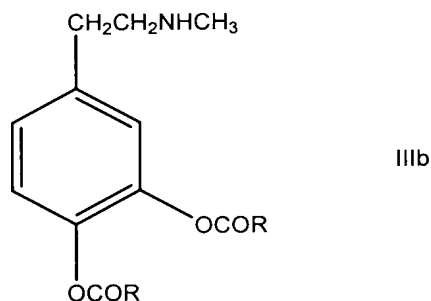
Buck and Carenzi, when considered alone or in combination, fail to provide a skilled artisan with sufficient motivation and guidance to particularly select the claimed ibopamine maleate salt having a molar ratio of ibopamine to maleate of 1:1 from either the tremendously large genus of compounds of formula IIIb and salts thereof, or the particularly preferred compounds of formula IIIb and salts thereof, described and exemplified in Buck, or the conventional ibopamine hydrochloride salt described and exemplified in Carenzi.

Applicants respectfully submit that even if sufficient motivation and guidance is considered to have been provided by Buck and/or Carenzi to direct a skilled artisan to arrive at the claimed ibopamine maleate salt having a molar ratio of ibopamine to maleate of 1:1, which clearly not the case, such a case of obviousness is rebutted by a showing of superior properties.

As shown by the comparative experimental data presented in Table 1 of the present specification, superior properties with respect to reduced swelling and lachrymation of the eye, as well as a desirable decrease in cornea opacity, are remarkably achieved after the administration of the claimed ibopamine maleate salt having a molar ratio of ibopamine to maleate of 1:1, as compared to the inferior properties of increased swelling and lachrymation of the eye, as well as an undesirable increase in cornea opacity, exhibited by the administration of the conventional ibopamine hydrochloride salt of Carenzi.

The fact that a claimed compound or species is encompassed by a prior art generic formula or genus is not sufficient by itself to establish a *prima facie* case of obviousness. *In re Baird*, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994); and *In re Jones*, 21 USPQ2d 1941, 1943 (Fed. Cir. 1992). The mere fact that a prior art generic formula or genus contains a small number of compounds or species does not alone create a *per se* rule of obviousness. *Id.*

Buck describes an amine compound or a salt thereof represented by the following general formula IIIb:



wherein each R substituent has 1 to 6 carbon atoms bound to the acyloxy group (See e.g., page 1, column 1, lines 22-40, and page 2, column 1, lines 46-53). Buck describes that salts of the bases may be formed by combining the bases with an acid, such as hydrochloric acid, sulfuric acid, phosphoric acid, maleic acid, succinic acid and the like by usual methods (See e.g., page 2, column 2, lines 3-6). Buck explicitly describes and exemplifies 31 particularly preferred amine compounds (See e.g., page 2, column 2, lines 10-73).

The number of positional isomers for each linear and branched alkyl group (omitting cycloalkyl groups) of an R substituent attached to the acyloxy group is shown in the following Table.

Carbon Atom No.	Positional Isomer No.
1	1
2	1
3	2
4	3
5	8
6	17
Total	32

Since there are two R groups, the total number of positional isomers is  $(32)(32) = 1,024$ . In addition, without considering the recitation “and the like,” there are at least 5 acids described in Buck (See e.g., page 2, column 2, lines 3-6). Accordingly, the approximate total number of possible salts of the amine compound of formula IIIb is at least  $(5)(1,024) = 5,120$ . Therefore, the amine salts of formula IIIb of Buck represents a tremendously large genus encompassing a plethora of amine compounds. Buck explicitly describes and exemplifies only 31 particularly preferred amine compounds (See e.g., page 2, column 2, lines 10-73).

An additional noteworthy distinction is that the present invention is directed to an ibopamine maleate salt having a “molar ratio of ibopamine to maleate of 1:1,” as opposed to a 2:1 ibopamine maleate salt obtained by the salification of both carboxylic acid groups of maleic acid with two moles of ibopamine. Unlike the claimed invention, Buck fails to disclose or suggest obtaining an ibopamine maleate salt having a molar ratio of ibopamine to maleate of 1:1, as presently claimed.

Unlike the claimed invention, Carenzi describes and exemplifies only the hydrochloride salt of ibopamine.

Buck and Carenzi, when considered alone or in combination, fail to provide sufficient motivation and guidance to direct a skilled artisan to particularly select the claimed ibopamine maleate salt having a molar ratio of ibopamine to maleate of 1:1 from either the tremendously large genus of compounds of formula IIIb and salts thereof, or the particularly preferred compounds of formula IIIb and salts thereof, described and exemplified in Buck, or the ibopamine hydrochloride salt described and exemplified in Carenzi.

Assuming *arguendo* that sufficient motivation and guidance is considered to have been provided by Buck and/or Carenzi to direct a skilled artisan to arrive at the claimed ibopamine maleate salt having a molar ratio of ibopamine to maleate of 1:1, which clearly not the case, such a case of obviousness is rebutted by a showing of superior properties.

As shown by the comparative experimental data presented in Table 1 of the present specification, superior properties with respect to reduced swelling and lachrymation of the eye, as well as a desirable decrease in cornea opacity, are remarkably achieved after the administration of the claimed ibopamine maleate salt having a molar ratio of ibopamine to maleate of 1:1, as compared to the inferior properties of increased swelling and lachrymation of the eye, as well as an undesirable increase in cornea opacity, exhibited by the administration of the conventional ibopamine hydrochloride salt of Carenzi.

Applicants submit that a skilled artisan would neither have been motivated, nor had a reasonably expectation of success for producing the claimed ibopamine maleate salt having a molar ratio of ibopamine to maleate of 1:1 for the purpose of improving tolerability, based on the limited disclosures of Buck and Carenzi, absent impermissible hindsight reconstruction, thereby precluding a *prima facie* case obviousness.

Withdrawal of this ground of rejection is respectfully requested.

The rejection of claims 4 and 5 under 35 U.S.C. § 112, second paragraph, and the objection of claims 6 and 11, are obviated by amendment with respect to the cancellation of said claims.

In conclusion, Applicants submit that the present application is now in condition for allowance and notification to this effect is earnestly solicited.

Respectfully submitted,

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A handwritten signature in black ink, appearing to read 'David P. Stitzel', is written over a horizontal line.

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